

Remarks

Claims 12-22, 24-26, and 32-43 were pending in the subject application. By this Amendment, claims 12-14 have been amended, claims 15-22, 24-26, and 32-43 have been cancelled, and new claims 44 and 45 have been added. The undersigned avers that no new matter is introduced by this Amendment. Support for the new claims and amendments can be found throughout the subject specification and in the claims as originally filed. Entry and consideration of the amendments presented herein is respectfully requested. Accordingly, claims 12-14, 44, and 45 are currently before the Examiner for consideration. Favorable consideration of the pending claims is respectfully requested.

Submitted herewith is a Request for Continued Examination (RCE) under 37 CFR §1.114 for the subject application.

Submitted herewith is a supplemental Information Disclosure Statement (IDS), accompanied by the form PTO/SB/08 and copies of the references listed therein. Applicants respectfully request that the references listed on the form PTO/SB/08 be considered and made of record in the subject application.

The Office Action indicates that the priority documents, provisional application numbers 60/481,738 and 60/522,180, do not provide adequate written support for one or more claims of the subject invention. Consequently, the Office Action indicates that the claims have an effective filing date of December 6, 2004. By this Amendment, claims 12-14 have been amended and new claims 44 and 45 have been added. Applicants respectfully submit that written support for claims 12-14 as amended and for new claims 44 and 45 can be found in application number 60/481,738, filed December 4, 2003. Support for claims 12-14 as amended can be found throughout provisional application number 60/481,738, including page 2, lines 7-16, (Summary of Invention); page 3, lines 29-35; page 9, lines 4-21; and page 13 (claim 1 and Abstract of the Disclosure). Support for claims 44 and 45 can be found, for example, at page 9, lines 10-14, and at page 13 (Abstract of the Disclosure) of application number 60/481,738. Therefore, claims 12-14, 44, and 45 are entitled to the filing date of application number 60/481,738, which is December 4, 2003.

Claims 12-19, 22, 24, 26, and 32-43 are rejected under 35 USC §103(a) as obvious over McCray *et al.* (U.S. Patent No. 7,297,786), Illum *et al.* (U.S. Patent No. 6,391,318), Mohapatra *et al.* (U.S. Patent Publication 2003/0068333), and Manoharan *et al.* (U.S. Patent Publication 2005/0106598). In addition, claims 20 and 21 are rejected under 35 USC §103(a) as obvious over McCray *et al.* (U.S. Patent No. 7,297,786), Illum *et al.* (U.S. Patent No. 6,391,318), Mohapatra *et al.* (U.S. Patent Publication 2003/0068333), and Manoharan *et al.* (U.S. Patent Publication 2005/0106598) as applied to claims 12-19, 22, 24, 26, and 32-43 above, and further in view of McSwiggen *et al.* (U.S. Patent 5,693,532) and Tuschl *et al.* (U.S. Patent Publication 2004/0259247). Furthermore, claim 25 is rejected under 35 USC §103(a) as obvious over McCray *et al.* (U.S. Patent No. 7,297,786), Illum *et al.* (U.S. Patent No. 6,391,318), Mohapatra *et al.* (U.S. Patent Publication 2003/0068333), and Manoharan *et al.* (U.S. Patent Publication 2005/0106598) as applied to claims 12-19, 22, 24, 26, and 32-43 above, and further in view of Prince *et al.* (U.S. Patent 5,290,540) and Huang *et al.* (U.S. Patent 6,586,579). Applicants respectfully traverse these grounds for rejection.

By this Amendment, claims 15-22, 24-26, and 32-43 have been cancelled, rendering the rejections of those claims moot. Furthermore, Applicants have amended claim 12 to recite a method for reducing the expression of a respiratory syncytial virus (RSV) gene and RSV viral titer in a human subject, comprising administering a vector to airway cells in the subject, wherein the vector comprises a nucleic acid sequence encoding a short interfering RNA (siRNA) targeted to a target nucleic acid sequence within the RSV NS1 gene or RSV NS1 transcript, and wherein the vector is administered in an effective amount to reduce expression of the RSV NS1 gene or NS1 transcript in the airway cells and reduce RSV titer in the subject. As indicated above, claims 12-14, 44, and 45 are entitled to the filing date of application number 60/481,738, which is December 4, 2003. Applicants note that each of the rejections under 35 USC §103(a) rely on the McCray *et al.* patent. As the earliest claimed priority date of the McCray *et al.* patent is July 9, 2004, which is after the effective filing date of the subject application, the McCray *et al.* patent is not available as prior art under 35 USC §103(a).

The other cited references (Illum *et al.* (U.S. Patent No. 6,391,318); Mohapatra *et al.* (U.S. Patent Publication 2003/0068333); Manoharan *et al.* (U.S. Patent Publication 2005/0106598); McSwiggen *et al.* (U.S. Patent 5,693,532); Tuschl *et al.* (U.S. Patent Publication 2004/0259247);

Prince *et al.* (U.S. Patent 5,290,540); and Huang *et al.* (U.S. Patent 6,586,579)) do not render obvious the claimed invention. None of these references teach or suggest a method for reducing the expression of a RSV gene and RSV viral titer in a human subject, comprising administering a vector to airway cells in the subject, wherein the vector comprises a nucleic acid sequence encoding a siRNA targeted to a target nucleic acid sequence within the RSV NS1 gene or RSV NS1 transcript. The Illum *et al.* patent is relied upon in the Office Action for disclosing chitosan nanoparticle compositions for delivering plasmids to respiratory cells *in vivo*. The Mohapatra *et al.* publication is cited in the Office Action for teaching that chitosan nanoparticles allow increased bioavailability of DNA. Manoharan *et al.* is relied upon in the Office Action for teaching that chitosan could be used to form nanoparticulate complexes with oligonucleotides. The Prince *et al.* patent is cited in the Office Action for teaching treatment of RSV infection by combining steroid treatment with administration of antivirals. The Huang *et al.* patent is cited for teaching that the use of inducible gene expression is advantageous, and that a steroid response control element is an inducible expression control element.

The McSwiggen *et al.* patent is cited in the Office Action for teaching methods of inhibiting the replication of RSV using ribozymes targeted to RSV NS1 and NS2 targets. The Tuschl *et al.* publication is cited for teaching that siRNAs provide greater gene silencing activities than ribozymes. The McSwiggen contains no empirical data, *in vitro* or *in vivo*, demonstrating that the ribozymes can be effectively delivered to airway cells *in vivo* such that expression of the RSV gene or transcript in the airway cells and RSV titer in the subject are reduced. Example 2 of Tuschl *et al.* demonstrates gene silencing in mammalian cells *in vitro*; however, there is no empirical evidence in the cited references that the siRNAs can be effectively delivered to airway cells *in vivo* such that expression of the RSV gene or transcript in the airway cells and RSV titer in the subject are reduced.

The cited references do not establish a clinical correlation between the disclosed procedures and reduction in RSV viral titer in the human airway. In contrast, as described in application number 60/481,738, Applicants demonstrated that delivery of a vector carrying an NS1-targeting siRNA to human A549 alveolar type-II epithelial cells resulted in reduced NS1 expression and reduced RSV production (Figures 1B, 2A, 2B, 3A, and 3B). Furthermore, Applicants demonstrated that the reduction of NS1 expression in these cells augmented expression of several interferon-response

genes (Figure 5 - STAT1, STAT6, IRF1, IRF3, and IRF7 genes), which contribute to the human antiviral response.

The cited references would not predictably generate success in delivering a vector comprising a nucleic acid sequence encoding an siRNA to airway cells, such that expression of a targeted RSV gene or transcript and RSV viral titer are reduced. The mere fact that references can be combined or modified does not render the resultant combination obvious unless the results would have been predictable to one of ordinary skill in the art. MPEP §2143.01. Obviousness does not require absolute predictability, however, at least some degree of predictability is required. Evidence showing there was no reasonable expectation of success may support a conclusion of nonobviousness. *In re Rinehart*, 531 F.2d 1048, 189 USPQ 143 (CCPA 1976); MPEP §2143.02. Accordingly, reconsideration and withdrawal of the rejections under 35 USC §103(a) is respectfully requested.

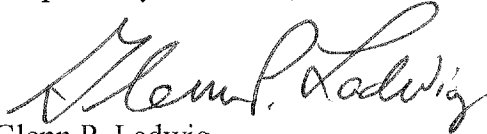
It should be understood that the amendments presented herein have been made solely to expedite prosecution of the subject application to completion and should not be construed as an indication of Applicants' agreement with or acquiescence in the Examiner's position.

In view of the foregoing remarks and amendments to the claims, Applicants believe that the currently pending claims are in condition for allowance, and such action is respectfully requested.

The Commissioner is hereby authorized to charge any fees under 37 CFR §§1.16 or 1.17 as required by this paper to Deposit Account 19-0065.

Applicants invite the Examiner to call the undersigned if clarification is needed on any of this response, or if the Examiner believes a telephonic interview would expedite the prosecution of the subject application to completion.

Respectfully submitted,



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Attachments: Request for Continued Examination  
Supplemental Information Disclosure Statement